

**REMARKS**

**INTRODUCTION:**

In accordance with the foregoing, claims 5, 21, and 25-27 have been amended. No new matter is being presented, and approval and entry are respectfully requested.

Claims 5-11, 21 and 24-27 are pending and under consideration. Reconsideration is respectfully requested.

**ENTRY OF RESPONSE UNDER 37 C.F.R. §1.116:**

Applicants request entry of this Rule 116 Response and Request for Reconsideration because:

(a) it is believed that the amendments of claims 5, 21, and 25-27 put this application into condition for allowance;

(b) the amendments were not earlier presented because the Applicants believed in good faith that the cited prior art did not disclose the present invention as previously claimed;

(c) the amendments of claims 5, 21, and 25-27 should not entail any further search by the Examiner since no new features are being added or no new issues are being raised; and/or

(d) the amendments do not significantly alter the scope of the claims and place the application at least into a better form for appeal. No new features or new issues are being raised.

The Manual of Patent Examining Procedures sets forth in §714.12 that "[a]ny amendment that would place the case either in condition for allowance or in better form for appeal may be entered." ( Underlining added for emphasis) Moreover, §714.13 sets forth that "[t]he Proposed Amendment should be given sufficient consideration to determine whether the claims are in condition for allowance and/or whether the issues on appeal are simplified." The Manual of Patent Examining Procedures further articulates that the reason for any non-entry should be explained expressly in the Advisory Action.

**REJECTION UNDER 35 U.S.C. §112:**

A. In the Office Action, at pages 2-3 and 5-7, claims 5-11, 21 and 24-27 were rejected under 35 U.S.C. §112, first paragraph, for the reasons set forth therein. This rejection is traversed and reconsideration is requested.

Although the Examiner submits that the terminology "a predetermined geometric distance" is new matter, it is respectfully submitted that on page 46, lines 6-22 (paragraph [0237] of the published application), the specification of the present invention sets forth:

In the aforementioned method of imparting correspondence, similar structures were successfully picked up by refining the candidates by taking into consideration such threshold conditions as geometrical relations such as distances among the elements in a point set, r.m.s.d. values and the number of nils, as well as attributes of constituent elements (kinds of amino acids in the case of a protein), and by finding optimum combinations. Still, extended periods of time are often required for calculating under certain shape conditions of the three-dimensional structure, the number of elements that constitute a point set, geometrical limitations and threshold values. Therefore, the calculation must be carried out at higher speeds. It, however, is difficult to establish a method that is capable of executing the processings at high speed under any condition. (emphasis added)

and on page 38, lines 6-21 (paragraph 0205] of the published application):

FIG. 22 is a diagram of system constitution of a device that displays the molecular structures in an overlapped manner according to the present invention. This device is constituted by a data base 80 in which are registered data related to the three-dimensional structures of substances, a data input unit 82 that reads the registered data and an input command from a user, a superposition calculation unit 84 that superposes the three-dimensional structures (three-dimensional coordinates) of the substance read from the data base 80 on the method of superposition discussed above in subsection 1 on page 28 of this application entitled "Various Methods of Determining Correspondence", 28 of this application r.m.s.d. values will become the smallest, and a graphic display unit 86 that displays the three-dimensional structures in an overlapped manner based on the calculated results. (emphasis added)

Hence, it is respectfully submitted that the terminology "a predetermined geometric distance" is not new matter. However, to further clarify the terminology, independent claims 5, 21, 25, 26, and 27 have been amended to change "predetermined minimized geometric distance" to recite ~~---predetermined minimized geometric root mean square distance values---~~ in accordance with the above-cited terminology wherein the method of superposition utilizes "r.m.s.d. values that will become the smallest." It is respectfully submitted that "minimized root mean square distance" is supported by the plain meaning of, e.g., the above citations from the specification of the present invention.

Thus, amended independent claims 5, 21, 25, 26, and 27 are submitted to be patentable under 35 U.S.C. §112, first paragraph. Since claims 6-11 and 24 depend, directly or indirectly, from amended claim 5, claims 6-11 and 24 are submitted to be patentable under 35 U.S.C. §112, first paragraph, for at least the reasons that amended claim 5 is submitted to be patentable under 35 U.S.C. §112, first paragraph.

B. In the Office Action, at pages 3-7, claims 5-11, 21 and 24 were rejected under

35 U.S.C. §112, first paragraph, for the reasons set forth therein. This rejection is traversed and reconsideration is requested.

For clarification, the claims as originally filed have been added to the specification as paragraphs [0318]-[0325]. No new matter was added.

As a general matter, the requirements of 35 U.S.C. §112, first paragraph, are that the written description demonstrate to one of ordinary skill in the art that the inventor is in possession of the invention itself. MPEP 2163.02. Additionally, when evaluating compliance with 35 U.S.C. §112, the original written description being reviewed includes not only the specification, but also the claims and drawings as filed. MPEP 2163.06. Further, the mere fact that the words used in the claims are not used in the specification *in haec verba* by using the same words does not necessarily mean that the specification does not describe the subject matter of the invention. MPEP 2163.02. As such, the requirements of 35 U.S.C. §112, first paragraph, are not that all details of an invention must be put forth in the written description using the same descriptive terminology, but instead whether the written description, including the claims as originally presented, provides sufficient details of the invention such that the disclosure reasonably conveys to one of ordinary skill in the art that the inventor had possession at the time of the later claimed subject matter.

On page 3 of the Office Action, the Examiner submitted that neither the specification nor the prior art provides guidance for how to determine if a combination of correspondence “satisfies” a condition. It is respectfully submitted that the restriction condition is set forth, e.g., in paragraph [0319], which is recited in part below for the Examiner’s convenience:

The restriction condition may include order relation of the elements in the first and the second point sets that are ordered and/or proximity in a geometric relationship among a plurality of elements close to each other. The restriction condition may include a condition such that a candidate for the combination of correspondence satisfies a threshold value condition. The restriction condition may include a condition such that an attribute value of each of the elements belonging to the first point set coincides with an attribute value of the corresponding element belonging to the second point set in a candidate for the combination of correspondence.

As noted above, the restriction condition may include an order relation of the elements, a geometric proximity relationship, a threshold value and/or a condition such that an attribute value of each of the elements belonging to the first point set coincides with an attribute value of the corresponding element belonging to the second point set in a candidate for the combination of correspondence. Hence, it is submitted to be clear to one skilled in the art what a restriction condition may be and how the “conditions” may be met or “satisfied.”

For example, in claim 5, the method includes:

generating, by a superposition calculating unit, a combination of correspondences, such as, e.g., are illustrated in FIGs. 13A-13D,

calculating, by the superposition calculating unit, a root mean square distance between the elements belonging to the first point set relating to the elements belonging to the second point set in the generated combination of correspondence;

determining, by the superposition calculating unit, based on the generated combination of correspondence and minimizing root mean square distance values, similar portions of the three dimensional structure of the predetermined amino acid sequence probe represented by the three-dimensional coordinates of the elements belonging to the first point set and the three-dimensional structure of the protein molecule target represented by the three-dimensional coordinates of elements belonging to the second point set; and

displaying, by a graphic display unit, the three-dimensional structures of the predetermined amino acid sequence and the protein molecule in an overlapped manner based on the generated combination of correspondence and minimized root mean square distance values.

wherein the first and second point sets, respectively, are sequence listings defining the predetermined amino acid sequence probe and the protein molecule target, respectively.  
(underlining added to facilitate understanding)

Thus, it is respectfully submitted that, in one embodiment of the present invention, the combinations of correspondences are generated, similar portions of the probe and target structures are determined, and three-dimensional structures of the probe and the target are displayed in an overlapped manner.

In another example, set forth in page 39, line 32 through line page 41, line 5, which is recited below for the Examiner's convenience, FIGs. 23A-23B, 24A-24B, 25 and 26 illustrate an embodiment of the present invention in which an amino acid sequence of calmodulin is compared with an amino acid sequence of troponin:

FIG. 23A shows an amino acid sequence of calmodulin, which is a protein, and FIG. 23B shows an amino acid sequence of troponin C. FIGS. 23A and 23B show in excerpts the amino acid sequences registered to the PDB. The amino acid sequence shown in FIG. 23A lacks amino acids that correspond to amino acid sequence Nos. 1-4 and 148 included in the ordinary amino acid sequence and, hence, the numbers are shifted. Hereinafter, these diagramed amino acid sequence numbers will be used. As shown in FIG. 24A, it is known from results of biochemical experiments that calmodulin can bind four  $\text{Ca}^{2+}$  as indicated by black rounds. Also, it is known that troponin C can bind two  $\text{Ca}^{2+}$  as indicated by black rounds in FIG. 24B. It is known that calmodulin has four places (sites) to bind  $\text{Ca}^{2+}$  in its amino acid sequence and among these amino acids of

sequence numbers 81-108 and 117-143 form skeletons similar to those of two sites to bind  $\text{Ca}^{2+}$  in troponin C. A protein is constituted by amino acids and it is known that its skeleton can be represented by the coordinates of atoms (Ca) that constitute the amino acids. FIG. 25 shows the results obtained when a spatially similar portion (a single site) is searched for based on the order of amino acid sequence using the  $\text{Ca}^{2+}$  binding site 81-108 of calmodulin as a probe. FIG. 25 indicates that the amino acid sequence numbers 96-123 in troponin C correspond to the  $\text{Ca}^{2+}$  binding sites 81-108 in calmodulin. These results are in agreement with the biochemically experimented results. FIG. 26 shows the results obtained when spatially similar portions (a plurality of sites) are searched for based on the order of amino acid sequence using  $\text{Ca}^{2+}$  binding site 81-108 and 117-143 in calmodulin as probes. FIG. 26 indicates that the amino acid sequence numbers 96-123 and 132-158 in troponin C correspond to the  $\text{Ca}^{2+}$  binding sites 81-108 and 117-143 in calmodulin. These results are in agreement with the biochemically experimented results, too. By using the apparatus of the present invention as described above, correspondence among the constituent elements of substances can be calculated in a manner such that the r.m.s.d. values are minimized in the three-dimensional structures of the substances. By displaying the corresponding portions in a superposed manner, therefore, it becomes possible to display the substances in a superposed manner in an optimum condition.

Thus, it is respectfully submitted that what a restriction condition may be, how the "conditions" may be met or "satisfied by a combination of correspondences, and how candidates are selected.

The Examiner submits that FIGs. 15 and 17 comprise flow charts which appear to correspond, at least in part, with the claimed method and apparatus. However, the Examiner submits that neither Figure sets forth any step of means for determining what conditions are required in order to determine a "yes" or "no" answer. It is respectfully submitted that FIGs. 15 and 17 each illustrate a question block that recites "SATISFY RESTRICTION CONDITION?" and that, as set forth above, in one embodiment, the restriction condition includes generating a combination based on minimized root mean square distance values between the first and second point sets, setting a predetermined threshold value and pruning a retrieval path if an attribute value of a candidate is greater than the predetermined threshold value, and determining that a point is a candidate if an attribute of an element of the first point set includes a type of an atom, an atomic group, and a molecule, a hydrophilic property, a hydrophobic property, or a positive or negative charge that coincides with an attribute of an element of the first point set, and refining the elements of the first and second point sets based on an attribute of the elements of the first and second point sets. Thus, it is submitted to be clear how to satisfy a restriction condition.

With respect to the Examiner's comments regarding FIG. 36, on page 49, lines 4-6, FIG. 36 is described as a diagram showing a division algorithm for the ordered point set B depending upon the spatial size of the point set A. That is, as illustrated in FIG. 36, in accordance with

claim 9, the condition includes a condition such that a candidate for the combination of correspondence satisfies a threshold condition: distances among points of the point sets A and B are calculated to prepare a distance table, a distance between a first point and a final point ( $a_1, a_m$ ) in the point set A is found from the distance table and is denoted as  $d$ , the point set B is divided to find from the distance table the one having a maximum  $j$  from among  $b_j$  that have a **distance of  $d \pm \alpha$  from  $b_i$  ( $i=1$ , in an initial state) and that satisfy  $m \leq j-i \leq 2m$  (this portion describes the threshold condition)** to obtain a point set  $B' = [b_i, b_{i+1}, \dots, b_{j-1}, b_j]$  (this is the set of candidates for combination of correspondence that satisfy the threshold value condition), and a correspondence is accomplished among the elements of point sets A,  $B'$  according to the method illustrated in FIGs. 17-21 in order to find correspondence that meets a predetermined limiting condition. Thus, FIG. 36 is submitted to be in proper form and to teach for how to perform the claimed method and how to use the apparatus.

With respect to the Examiner's comments regarding FIG. 37, on page 50, lines 16-18, FIG. 37 is described as illustrating that it is possible to divide the ordered point set B depending on the spatial size of the point set A. In this embodiment, the points are related to each other after the search space of three-dimensional structures is divided. Thus, here again in accordance with claim 9, the condition includes a condition such that a candidate for the combination of correspondence satisfies a threshold condition: distances among points of the points sets A and B are calculated to prepare a distance table, a distance between a first point and a final point ( $a_1, a_m$ ) in the point set A is found from the distance table, and is denoted as  $d$ , the point set B is divided, finding from the distance table the one having a maximum  $j$  from among  $b_j$  that have a **distance of  $d \pm \alpha$  from  $b_i$  ( $i=1$ , in initial state) and that satisfy  $m \leq j-i \leq 2m$  (the threshold condition)** to obtain a point set  $B' = [b_i, b_{i+1}, \dots, b_{j-1}, b_j]$  (this is the set of candidates for combination of correspondence that satisfy the threshold value condition), and accomplishing correspondence among the elements of point sets A,  $B'$  according to the method explained with reference to FIGs. 17 to 21, in order to find correspondence that meets a predetermined limiting condition. That is, a distance is found across two points at both ends of the point set A, and the point set B is divided by this distance to reduce the search space and to shorten the time for calculation. Moreover, at the time of advancing to the next search space, the next search space is set by taking into consideration the number of elements of the point set A that serve as search keys, so that the search spaces will not be overlapped and the same solution will not be calculated many times. Thus, FIG. 37 is submitted to be in proper form and to teach for how to perform the claimed method and how to use the apparatus.

As admitted by the Examiner, the prior art of Pantoliono does not teach that any

conditions" must be met or satisfied in order to generate the comparison and/or perform the root mean square calculation. Thus, it is respectfully submitted that Pantoliono does not teach or suggest the present claimed invention.

As noted by the Examiner, the level of skill in the art is considered to be high. However, it is respectfully submitted that, as noted above, the method and apparatus of the present invention are clearly described, and one skilled in the art does not need to guess at the parameters necessary to perform such a determination or calculation, and that undue experimentation would not be needed by one skilled in the art to generate a combination of correspondence satisfying a condition.

The Examiner submits that none of the rmsd, the comparison of attributes and the determination of whether a predetermined threshold value has been reached is order to provide an optimal combination appear to be the "condition" which must be satisfied. It is respectfully submitted that, The Examiner did not fully understand the present claimed invention. The restriction conditions have been clarified above. As noted above, for example, the condition may include a condition such that a candidate for the combination of correspondence satisfies a threshold condition (see, e.g., FIGs. 36 and 37) to obtain a set B', and the elements of point sets A, B' are then utilized according to the method explained with reference to FIGs. 17 to 21. It is respectfully submitted that one skilled in the art would not require undue experimentation to implement the present claimed method or apparatus.

The Examiner submits that claims 5, 21 and 24-27 recite generating a combination of correspondence satisfying a "condition" and that the specification does not disclose what requirements must be met in order for a combination of correspondence to "satisfy" a condition. As noted above and as recited in paragraph [0319] of the specification, the restriction condition may include order relation of the elements in the first and the second point sets that are **ordered and/or proximity in a geometric relationship among a plurality of elements close to each other**. The restriction condition may include a condition such that a **candidate for the combination of correspondence satisfies a threshold value condition**. The restriction condition may include a condition such that **an attribute value of each of the elements belonging to the first point set coincides with an attribute value of the corresponding element belonging to the second point set in a candidate for the combination of correspondence**. Claim 6 recites: "The method of claim 5, wherein the condition includes **order relation** of the elements in the first and the second point sets that are ordered" (emphasis added). Claim 7 recites: "The method of claim 6 wherein the condition includes **proximity in a geometric relationship among a plurality of elements close to each other**" (emphasis

added), and claim 8 recites: "The method of claim 6 wherein the condition includes **proximity in a geometric relationship among a plurality of elements close to each other** (emphasis added). Claim 9 recites: "The method of claim 5, wherein the condition includes a condition such that **a candidate for the combination of correspondence satisfies a threshold value condition**" (emphasis added), and claim 10 recites: "The method of claim 6, wherein the condition includes a condition such that **a candidate for the combination of correspondence satisfies a threshold value condition**" (emphasis added). Claim 11 recites: "The method of claim 5, wherein the condition includes **a condition such that an attribute value of each of the elements belonging to the first point set coincides with an attribute value of the corresponding element belonging to the second point set in a candidate for the combination of correspondence.**"

Thus, it is respectfully submitted that , in contrast to the Examiner's submission, the claims and the specification define the restriction conditions, i.e., the requirements that must be met in order for a combination of correspondence to satisfy a condition are set forth in the specification and the claims as noted above, for example, as recited with respect to FIGs. 36-37 and FIGs. 17-21.

The Examiner submitted that claims 5, 21 and 24-27 limit an attribute of an element of a first point set to include (comprise) a type of atom, an atomic group, "and" a molecule, hydrophobic property "or" a positive or negative charge. and that the combination of "and" and "or" limiting the terms of the list renders unclear whether the first point set is intended to comprise ALL of the attributes listed (as would be indicated by the term ---and--- between the last two elements of the list only) or any one of the attributes listed (as would be indicated by the term ---or--- between the last two elements of the list only), or intends some combination of the attributes listed.

For clarity, independent claims 5, 21, 25, 26 and 27 have been amended to recite, in part: "...determining that a point is a candidate if an attribute of an element of the first point set includes a type of an atom, an atomic group, ~~and~~ a molecule, a hydrophilic property, a hydrophobic property, or a positive or negative charge that coincides with an attribute of an element of the first point set." Hence amended claims 5, 21, 25, 26 and 27 are now submitted to be in form for allowance under 35 U.S.C. §112, first paragraph.

## CONCLUSION:

In accordance with the foregoing, it is respectfully submitted that all outstanding objections and rejections have been overcome and/or rendered moot, and further, that all



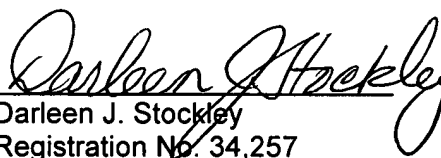
pending claims patentably distinguish over the prior art. Thus, there being no further outstanding objections or rejections, the application is submitted as being in condition for allowance which action is earnestly solicited. At a minimum, this Amendment should be entered at least for purposes of Appeal as it either clarifies and/or narrows the issues for consideration by the Board.

If the Examiner has any remaining issues to be addressed, it is believed that prosecution can be expedited and possibly concluded by the Examiner contacting the undersigned attorney for a telephone interview to discuss any such remaining issues.

If there are any underpayments or overpayments of fees associated with the filing of this Amendment, please charge and/or credit the same to our Deposit Account No. 19-3935.

Respectfully submitted,

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